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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Mark T. KEATING et al.

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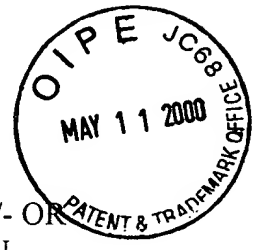

Examiner: S-L. Chen

Group Art Unit: 1633

For: MICE WHICH ARE +/- OR -/- FOR THE ELASTIN GENE AS MODELS FOR VASCULAR DISEASE

DECLARATION OF MARK T. KEATING

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Mark T. Keating declare as follows:

1. I am a coinventor of the above-identified application.

2. My educational background and employment are shown in my Curriculum Vitae, attached hereto as Exhibit 1.

3. I am a co-author of each of the following two publications, which have been cited in the above-identified application:

Li et al. (1998). *J. Clin. Invest.* 102:1783-1787.

Li et al. (1998). *Nature* 393:276-280.

4. I believe that I, along with Dean Y. Li, am an original, first and joint inventor of the subject matter described and claimed in the above-identified application, and of the subject matter disclosed in the two publications identified in paragraph 3 above, specifically the subject matter directed to mice with mutated or missing elastin genes and to methods of using the mutant mice such as to screen for drugs.

5. It is customary practice to include as authors on papers those individuals who have been involved with the reported project in some manner, e.g., a research associate, laboratory technician, or someone who has provided materials or laboratory space (a collaborating scientist). The latter individual does not make any other contribution to the research. The research associates or laboratory technicians work under the direction and supervision of the supervising

professor, post-doctoral associates, or research instructor. It is also customary practice to include all individuals who contributed to different aspects of the subject matter disclosed in a paper.

6. The following is a list of the co-authors of the papers set forth in paragraph 3 above, and their position relative to the reported research:

Li et al. (1998). *J. Clin. Invest.* 102:1783-1787

Dean Y. Li - Co-applicant of the present application

Gilles Faury - This author is a postdoctoral fellow and performed assays of the elasticity of blood vessels of the mutated mice but was not involved with the making of the mutant mice.

Douglas G. Taylor - This author is a technician and worked under the direction of the Applicants of the present invention. He made sections of blood vessels but was not involved in making the mutant mice.

Elaine C. Davis - This author performed electron microscopy to prepare electron micrographs of arteries taken from mice but was not involved in the preparation of the mutant mice.

Walter A. Boyle - This author did not perform any work described in the Li et al. publication nor did he contribute intellectually to the publication. This author supplied equipment which was used to assay the elasticity of tissue samples.

Robert P. Mecham - Gilles Faury (discussed above) is a postdoctoral fellow in Robert P. Mecham's laboratory. Robert P. Mecham is a coauthor of the published paper because a member of his laboratory performed some of the work presented in the paper. Dr. Mecham did not perform any of the work presented in the Li et al. publication nor did he contribute intellectually to any of the work presented in the Li et al. publication.

Peter Stenzel - This author provided human tissue sections from persons with SVAS. He did not perform any of the mouse studies nor did he contribute intellectually to any of the studies reported in the Li et al. publication.

Beth Boak - Ms. Boak is a technician who performed molecular biology experiments such as Northern blots under the direction of the two Applicants of the present application. She did not contribute to the making of the mutant mice nor did she contribute to the intellectual process of the experiments reported in the Li et al. publication.

Mark T. Keating - Dr. Keating is a co-applicant of the present application.

Li et al. (1998). *Nature* 393:276-280

Dean Y. Li - Co-applicant of the present application

Benjamin Brooke - Mr. Brooke was a medical student who helped to characterize the mutant mice but did not participate intellectually in the making of these mice nor in determining possible uses for the mice.

Elaine C. Davis - This author performed electron microscopy to prepare electron micrographs of arteries taken from mice but was not involved in the preparation of the mutant mice.

Robert P. Mecham - Gilles Faury (discussed above) is a postdoctoral fellow in Robert P. Mecham's laboratory. Robert P. Mecham is a coauthor of the published paper because a member of his laboratory performed some of the work presented in the paper. Dr. Mecham did not perform any of the work presented in the Li et al. publication nor did he contribute intellectually to any of the work presented in the Li et al. publication.

Lise K. Sorensen - Ms. Sorensen is a technician who performed experiments under the direction of Mark T. Keating and Dean Y. Li. Specifically, she performed some of the immunohistochemistry experiments reported in this publication. She did not contribute to the making of the mutant mice nor did she contribute intellectually to the uses for the mice.

Beth Boak - Ms. Boak is a technician who performed molecular biology experiments such as Northern blots under the direction of the two Applicants of the present application. She did not contribute to the making of the mutant mice nor did she contribute to the intellectual process of the experiments reported in the Li et al. publication.

Ernst Eichwald - Dr. Eichwald is a pathologist who looked at slides of tissue samples to determine the pathology of the tissue. He did not help to make the mutant mice nor did he contribute intellectually to the making or using of the mice.

Mark T. Keating - Dr. Keating is a co-applicant of the present application.

The declarant further states that the above statements were made with the knowledge that willful false statements and the like are punishable by fine and/or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that any such willful false statement may jeopardize the validity of this application or any ~~patent~~ resulting therefrom.

Dated: May 2, 2000

Mark T. Keating

CURRICULUM VITAE

Name **Mark T. Keating, M.D.**

Address Howard Hughes Medical Institute
Eccles Institute of Human Genetics
University of Utah
15N 2030E, Suite 6110B
Salt Lake City, UT 84112-5330

Phone: 801-581-8904 Fax: 801-585-7423
email: mark@howard.genetics.utah.edu

Date and Place of Birth May 6, 1954; Lampasas, Texas

Marital status Married, 2 children

Education

1976 A.B.	Princeton University
1980 M.D.	The Johns Hopkins University, School of Medicine

Postdoctoral Training

1980-1983 Resident in Medicine, The Johns Hopkins Hospital
1983-1985 Fellow in Cardiology, University of California, San Francisco

Research Fellowship

1985-1989 NIH Physician Scientist Award, laboratory of Lewis T. Williams, M.D., Ph.D., University of California, San Francisco

Licensure and Certification

1980 Maryland License (#D25386)
1983 California License (#C040943)
1983 American Board of Internal Medicine (#090674)
1985 ABIM Subspecialty Board of Cardiovascular Disease (#90674)
1989 Utah License (#0991910220)

Academic Appointments

1985-1987 Instructor, Department of Medicine, University of California, San Francisco

1987-1989	Assistant Professor, Department of Medicine, University of California, San Francisco
1989-1993	Assistant Professor, Department of Medicine and Department of Human Genetics, University of Utah
1989-1994	Member, Program in Human Molecular Biology & Genetics, University of Utah
1993-1995	Associate Professor with Tenure, Department of Medicine and Department of Human Genetics, University of Utah
1994-1997	Associate Investigator, Howard Hughes Medical Institute
1995-Present	Professor, Department of Medicine and Department of Human Genetics, University of Utah
1996-Present	L. George Veasy Presidential Endowed Chair in Pediatric Cardiology
1997-Present	Investigator, Howard Hughes Medical Institute
1998-Present	Adjunct Professor, Department of Pediatrics, University of Utah

Awards and Honors

1990	Syntex Scholars Award
	Dee Lecture, Vanderbilt University
1995	Bristol-Myers Squibb Unrestricted Grant for Cardiovascular and Metabolic Diseases Research
	Dean's Distinguished Seminar, University of Colorado
1997	Basic Research Prize, American Heart Association
	Kober Lecture, American Association of Physicians
1998	Edgar A. Haber Cardiovascular Medicine Research Award, American Heart Association
	Ira and Jean Belfer Lecture, Johns Hopkins University
1999	Young Investigator Award, Western Society of Clinical Investigation
	Cardiovascular Research Award, The Robert J. and Claire Pasarow Foundation
	Society of Scholars, The Johns Hopkins University
1999	Carl Vernon Moore Lecturer, Washington University School of Medicine

Professional Societies

1987-Present	American Heart Association, Council on Basic Sciences
1987-Present	American Federation for Clinical Research
1990-Present	American Society of Human Genetics
1994-Present	American Society for Clinical Investigation
1995-Present	Executive Committee, American Heart Association, Council on Basic Sciences
1995-Present	Society of General Physiologists
1995-Present	Molecular Medicine Society
1996-Present	American Association of Physicians

Editorial Boards

1994	Trends in Cardiovascular Medicine
1995	Circulation

Ad hoc Reviewer
Science, Nature Genetics, Journal of Biological Chemistry, Journal of Clinical Investigation, Proceedings of the National Academy of Science, USA, New England Journal of Medicine, Circulation, Journal of American College of Cardiology, Circulation Research, American Journal of Physiology, Nature Medicine, Human Molecular Genetics

Teaching Experience

1990	Attending in Cardiology, University Hospital
1991	Human Genetics 602, Advanced Topics in Genetics
1992	Attending in Internal Medicine, VAMC
	Attending in Internal Medicine, University Hospital
1993	Attending in Cardiology, University Hospital
1994	Attending in Cardiology, University Hospital
	Attending in Internal Medicine, University Hospital
1995	Attending in Internal Medicine, University Hospital
	Attending in Internal Medicine, University Hospital
1997	Attending in Internal Medicine, University Hospital
1998	Attending in Internal Medicine, University Hospital

Institutional Committees

1991-Present	University of Utah Tenured Faculty Appeals Committee
1994-Present	Chair, Oversight Committee for the University of Utah Fluorescence In Situ Hybridization Core Facility
1994-Present	Committee for the University of Utah cDNA Library Core Facility
1995-Present	Human Genetics Graduate Student Committee
1995-1998	Chair, Eccles Cardiovascular Research Fundraising Committee
1995-Present	Coordinator, University of Utah M.D./Ph.D. Program
1995-1998	Elected Member, University of Utah Research Council

Extramural Peer Review Committees

1991-Present	Ad hoc NIH Reviewer
1994-1995	American Heart Association Grant-in-Aid Reviewer
1995-Present	Ara Parseghian Medical Research Foundation Board
1999	Board of Scientific Counselors, NIH/NHLBI Intramural Program

Current Extramural Funding

Howard Hughes Medical Institute, 1994 - 2004
Isolating long QT syndrome genes, NIH R01 HL46401, 4/97-3/02
Elastin in SVAS and Williams syndrome, NIH R0150343, 7/93-6/01
Genotype/Phenotype correlations in Williams syndrome, NIH R01 NS35102, 9/97-3/05
SCOR in Sudden Death, NIH P50 HL52338, 1/00-12/04
SCOR in Heart Failure, NIH P50 HL53373, 1/00-12/04

Research Interests

1. Organ regeneration
2. The molecular and cellular mechanisms of cardiac arrhythmias
3. The role of elastin in vascular development and disease
4. The molecular basis of Williams syndrome
5. The molecular genetics of dilated cardiomyopathy

Invited Lectures at Symposia

1991

American Heart Association National Meeting, "Symposium on Molecular Genetics of Cardiovascular Disease"
American Association for Clinical Chemistry, Conference on Nucleic Acids
American Heart Association, "Molecular and Cellular Biology of the Cardiac Myocyte"

1992

American College of Cardiology National Meeting, Annual Symposium for Directors of Cardiology Training Programs
International Congress of Cardiology, "Contributions of Molecular Biology to Cardiology"
American Society for Clinical Pharmacology and Therapeutics Annual Meeting, "Potassium Channels as Targets for Drug Action"
American College of Physicians Annual Meeting

1993

American Heart Association-Asilomar Conference on the Cardiac Myocyte
Gordon Research Conference on Elastin
American Society for Human Genetics National Meeting, "Molecular Genetics of Cardiovascular Disease"
Nexagen, Inc., Boulder, Colorado
American Heart Association National Meeting, "Cardiovascular Disease: Molecular Strategies for the 90's"

1994

Electrophysiology Board Review Course
Pine Ridge Conference on Thrombosis
National FASEB meeting "Genetic Models of Cardiovascular Disease"
Cardiostim, Nice, France
National Meeting of the Williams Syndrome Association
Annual Meeting of the Society of General Physiologists
Bristol-Myers Squibb Symposium on Cardiovascular Biology
Sequana, Inc., La Jolla, California

1995

American Heart Association Symposium, "Molecular, Cellular and Functional Aspects of Cardiovascular Development"
National Institutes of Health Symposium on Basement Membranes
Gordon Research Conference on Elastin
Chiron, Inc., Emeryville, California
Chiron/Ciba Cardiovascular Symposium
Sequana, Inc., La Jolla, California
Cardiac Electrophysiology Society
Bristol-Myers Squibb Pharmaceutical Research Institute
Howard Hughes Medical Institute Scientific Meeting

1996

Keynote Speaker, Association of University Cardiologists
Keystone Symposia on Molecular and Cellular Biology
Mercator Genetics, San Francisco, California
Co-Chair, Biomedicine '96 (AAP/ASCI/AFCR), "Ion Transport and Disease"
Bristol-Myers Squibb Pharmaceutical Research Institute, Cardiovascular Colloquium
International Society for Heart Research, "Cellular Signaling in the Cardiovascular System"
American Heart Association, Scientific Conference on the Molecular Biology of the Normal, Hypertrophied, and Failing Heart
Plenary Speaker, American Heart Association
Howard Hughes Medical Institute Scientific Meeting

1997

National Advisory Research Council, National Institutes of Health
Kober Lecture, American Association Physicians
Chairman, "LQT Syndrome: Patients and Paradigms," National Institutes of Health
American Thoracic Society, Vascular Disease Workshop

Gordon Conference on Elastin and Elastic Tissue
International Congress of Biochemistry and Molecular Biology
Plenary Speaker, American Heart Association
Howard Hughes Medical Institute Scientific Meeting

1998

Cloister Scholars Lecture, Howard Hughes Medical Institute-National Institutes of Health Lecture
Plenary Speaker, American Heart Association
Keynote Speaker, 62nd Annual Meeting of Japanese Circulation Society, "Molecular and Cellular Mechanisms of Cardiac Arrhythmias" and Plenary session, "Molecular Mechanisms of Cardiovascular Disease"
Keystone Conference, "Molecular Genetic Insights Into Arrhythmias and Vascular Disease"
Keynote Speaker, Gordon Conference, Cardiac Regulatory Mechanisms
Howard Hughes Medical Institute Scientific Meeting

1999

Plenary Speaker, American Heart Association
Howard Hughes Medical Institute Scientific Meeting
Howard Hughes Medical Institute Scientific Review
American Heart Association
Heart Failure Society of America

2000

Keystone Conference, "Molecular Biology of the Cardiovascular System"

Invited Lectures to Universities and Research Institutions (1991 - in chronological order)

Duke University
University of Texas Southwestern Medical Center
University of Alabama at Birmingham
University of California, San Francisco
University of Michigan
University of Toronto
Vanderbilt University
University of Chicago
Washington University
Harvard Medical School
The Rockefeller University
University of California, San Francisco
University of California, San Diego
University of California, Los Angeles

Stanford University
University of Colorado School of Medicine
Harvard Medical School
Johns Hopkins University, School of Medicine
University of Texas Southwestern Medical Center
Harvard Medical School
Johns Hopkins University, School of Medicine
University of California, San Francisco
University of Pennsylvania

Symposia Directorships

6th Annual Bristol-Myers Squibb Symposium, Molecular Physiology of Ion Channels, March 19-20, 1998

Previous Fellows/Trainees

Postdoctoral fellows
Qing Wang, Ph.D., currently Assistant Professor at The Cleveland Clinic Foundation
Dean Li, M.D., Ph.D., currently Assistant Professor in Cardiology and investigator in The
Program in Human Molecular Biology & Genetics at the University of Utah
Timothy Olson, M.D., currently Assistant Professor in Pediatrics at the Mayo Clinic.
Xiaojun Lu, Ph.D., currently a postdoctoral fellow at the University of Colorado
Zhengyi Wang, Ph.D., currently a postdoctoral fellow at the University of Iowa
Xun Meng, Ph.D., currently Technician at Orion Genomics
Lisa Urness, Ph.D. currently postdoctoral fellow at the University of Utah
Chris McGann, M.D., currently Fellow in Dept. of Cardiology at the Univ. Utah

Students
Mark Curran, Ph.D. "Molecular genetics of the long QT syndrome",
currently Program Scientist/Head of Genetics, ICAgen, Inc.
Amanda Ewart, Ph.D. "Molecular genetics of Williams syndrome",
currently a postdoctoral fellow in cancer genetics at the UCSF Cancer Center
University of California at San Francisco
Igor Splawski, Ph.D. "Molecular Basis for Cardiac Arrhythmia", currently a postdoctoral fellow in the laboratory of Dr. Mark Keating
Michael Frangiskakis, Ph.D. "Lim Kinase1 and the Williams Syndrome Cognitive Profile", currently enrolled in medical school at the University of Michigan

Present Trainees/Support

Postdoctoral fellows
Shannon Odelberg, Ph.D. (NIH)
Sutip Navankassatusas, Ph.D. (HHMI)
Kenneth Poss, Ph.D. (The Helen Hay Whitney Foundation)
Sanjay Jha, M.D. (NIH Training Grant)

Students
Tamilla Nechiporuk, graduate student – Molecular Biology
Alex Nechiporuk, graduate student – Molecular Biology
Eric Hempel, graduate student – Molecular Biology

Patents

1993 Diagnosis and treatment of supravalvular aortic stenosis and Williams syndrome (Keating MT, Leppert MF, Morris CA). Patent No. 5,840,489. Date of Patent: November 24, 1998.

1996 Diagnosis of Williams syndrome and Williams syndrome cognitive profile by analysis of the presence or absence of a Lim-Kinase gene (Keating MT, Morris CA). Patent No: 5,858,662. Date of Patent: Jan. 12, 1999.
Diagnosis of Williams syndrome (Keating MT, Morris CA, Leppert MF) Patent No. 5,650,282. Date of Patent: July 22, 1997.

1996 KVLQT1-A long QT syndrome gene (Keating MT, Wang Q, Curran ME, Landes GM, Connnors TD). Pending.

1996 KVLQT1-A long QT syndrome gene which encodes KVLQT1 which coassembles with minK to form cardiac I_{ks} potassium channels (Keating MT, Sanguinetti, MC). Pending.

1996 Long QT syndrome genes (Keating MT, Curran ME, Wang, Q). Patent No. 5,599,673. Date of Patent: February 4, 1997.

1997 Mutations in the KCNE1 gene encoding human minK which cause arrhythmia susceptibility thereby establishing KCNE1 as an LQT gene (Keating MT, Sanguinetti MC). Pending.

1998 Cardiac actin ACTC is a dilated cardiomyopathy gene (Keating MT, Olson TM). Pending.

1998 Elastin disruption causes obstructive vascular disease (Keating, MT and Li, Dean Y). Pending.

PUBLICATIONS

Peer-Reviewed Primary Publications

Keating MT and Bonner JT. Negative chemotaxis in cellular slime molds. ***Journal of Bacteriology,*** 1977; 130:144-147.

Keating MT and Williams LT. Processing of the platelet-derived growth factor receptor; Biosynthetic and degradation studies using anti-receptor antibodies. ***Journal of Biological Chemistry,*** 1987; 262:7932-37.

Williams LT, Escobedo JA, Keating MT and Coughlin SR. The stimulation of paracrine and autocrine mitogenic pathways by the platelet-derived growth factor receptor. ***Journal of Cellular Physiology Supplement,*** 1987; 5:27-30.

Kass DA, Traill TA, Keating M, Altieri PI, and Maughan, L. Abnormalities of dynamic ventricular shape change in patients with aortic and mitral valvular regurgitation:

assessment by Fourier shape analysis and global geometric indexes. ***Circulation Research,*** 1987; 62:127-138.

Escobedo JA, Keating MT, Ives HR and Williams LT. Platelet-derived growth factor receptors expressed by cDNA transfection couple to a diverse group of cellular responses associated with cell proliferation. ***Journal of Biological Chemistry,*** 1988; 263:1482-7.

Keating MT and Williams LT. Autocrine stimulation of intracellular PDGF receptors in v-*sis*-transformed cells. ***Science,*** 1988; 239:914-6.

Keating MT, Escobedo JA and Williams LT. Ligand activation causes a phosphorylation dependent change in platelet-derived growth factor receptor conformation. ***Journal of Biological Chemistry,*** 1988; 263:12805-8.

Keating MT, Escobedo JA, Fantl WJ and Williams LT. Ligand activation causes a phosphorylation-dependent change in platelet-derived growth factor receptor conformation. ***Transactions of the American Association Physicians,*** 1988; 101:24-32.

Keating MT, Harryman CC and Williams LT. Platelet-derived growth factor receptor inducibility is acquired immediately after translation and does not require glycosylation. ***Journal of Biological Chemistry,*** 1989; 264:9129-32.

Harsh GR, Keating MT, Escobedo JA and Williams LT. Platelet-derived growth factor (PDGF) autocrine components in human tumor cell lines. ***Journal of Neurological Oncology,*** 1990; 8:1-12.

Keating M, Atkinson D, Dunn C, Timothy K, Vincent GM and Leppert, M. Linkage of a cardiac arrhythmia, the long QT syndrome, and the Harvey *ras*-1 gene. ***Science,*** 1991; 252:704-6.

Keating M, Dunn C, Atkinson D, Timothy K, Vincent GM and Leppert M. Consistent linkage of the long-QT syndrome to the Harvey *ras*-1 locus on chromosome 11. ***American Journal of Human Genetics,*** 1991; 49:1335-9.

Curran ME, Landes GM and Keating MT. Molecular cloning, characterization and genomic localization of a human potassium channel gene. ***Genomics,*** 1992; 12:729-37.

Vincent GM, Timothy KW, Leppert M and Keating M. The spectrum of symptoms and QT intervals in carriers of the gene for the long-QT syndrome. ***New England Journal of Medicine,*** 1992; 327:846-52.

Ewart AK, Morris CA, Ensing GJ, Loker J, Moore C, Leppert M and Keating, M. A human vascular disorder, supravalvular aortic stenosis, maps to chromosome 7. ***Proceedings of the National Academy of Science (USA),*** 1993; 90:3226-30.

Curran ME, Atkinson DL, Ewart AK, Morris CA, Leppert MF and Keating MT. The elastin gene is disrupted by a translocation associated with supravalvular aortic stenosis. ***Cell,*** 1993; 73:159-68.

Ewart AK, Morris CA, Atkinson D, Jin W, Sternes K, Spallone P, Stock AD, Leppert M and Keating MT. Hemizygosity at the elastin locus in a developmental disorder,Williams syndrome. ***Nature Genetics,*** 1993; 5:11-16.

Keating M. Evidence of genetic heterogeneity in the long QT syndrome. ***Science,*** 1993; 260:1960-1962.

Curran M, Atkinson D, Timothy K, Vincent GM, Moss AJ, Leppert M and Keating M. Locus heterogeneity of autosomal dominant long QT syndrome. ***Journal of Clinical Investigation,*** 1993; 92:799-803.

Phromchotikul T, Browne DL, Curran ME Keating MT and Litt M. Dinucleotide repeat polymorphism at the KCNA5 locus. ***Human Molecular Genetics,*** 1993; 2:1512.

Ewart A, Jin W, Atkinson D, Morris CA and Keating MT. Supravalvular aortic stenosis associated with a deletion disrupting the elastin gene. ***Journal of Clinical Investigation,*** 1994; 93:1071-77.

Wang Q and Keating MT. Isolation of P1 insert ends by direct sequencing. ***Biotechniques,*** 1994; 17:282-4.

Jiang, C, Atkinson, D, Towbin, JA, Splawski, I, Lehmann, M, Li, H, Timothy, K, Taggart, RT, Schwartz, PJ, Vincent, GM, Moss, AJ and Keating, MT. Two long QT syndrome loci map to chromosomes 3 and 7 with evidence for further heterogeneity. ***Nature Genetics,*** 1994; 8:141-7.

Curran, M and Keating, M. A polymorphic dinucleotide repeat in the second intron of HUMCLC. ***Human Molecular Genetics,*** 1994; 3:2264.

Marks ML, Whisler SL, Clericuzio C and Keating M. A new form of long QT syndrome associated with syndactyly. ***Journal of American College of Cardiology,*** 1995; 25:59-64.

Curran, ME, Splawski, I, Timothy, KW, Vincent, GM, Green, ED, and Keating, MT. A molecular basis for cardiac arrhythmia: *HERG* mutations cause long QT syndrome. ***Cell,*** 1995; 80:795-803.

Wang Q, Shen J, Splawski I, Atkinson D, Li Z, Robinson JL, Moss AJ, Towbin JA and Keating MT. *SCN5A* mutations associated with an inherited cardiac arrhythmia, long QT syndrome. ***Cell,*** 1995; 80:805.

Sanguinetti MC, Jiang C, Curran ME and Keating MT. A mechanistic link between an inherited and an acquired cardiac arrhythmia: *HERG* encodes the I_{Kr} potassium channel. ***Cell,*** 1995; 81:299-307.

Nickerson E, Greenberg F, Keating MT, McCaskill C and Shaffer LG. Deletions of the elastin gene at 7q11.23 occur in approximately 90% of patients with Williams syndrome. ***American Journal of Human Genetics,*** 1995; 56:1156-61.

Lowery MC, Morris CA, Ewart AK, Brothman LJ, Zhu XL, Leonard, CO, Carey JC, Keating M and Brothman AR. Strong correlation of elastin deletions, detected by FISH with Williams syndrome: evaluation of 235 patients. ***American Journal of Human Genetics,*** 1995; 57:49-53.

Landes GM, Curran ME and Keating MT. Molecular characterization and refined genomic localization of three human potassium ion channel genes. ***Cytogenetic Cell Genetics,*** 1995; 70:280.

Wang Q, Shen J, Li Z, Timothy K, Vincent GM, Priori S, Schwartz PJ and Keating MT. Cardiac sodium channel mutations in patients with long QT syndrome, an inherited cardiac arrhythmia. ***Human Molecular Genetics,*** 1995; 4:1603-7, 1995.

Marks ML, Trippel DL, and Keating MT. Long QT syndrome associated with syndactyly identified in females. ***American Journal of Cardiology,*** 1995; 76:744-45.

Moss AJ, Wojciech Z, Benhorin J, Locati EH, Hall WJ, Robinson JL, Schwartz PJ, Towbin JA, Vincent GM, Lehmann MH, Keating MT, MacCluer J and Timothy KW. ECG T-wave patterns in genetically distinct forms of the hereditary long QT syndrome. ***Circulation,*** 1995; 92:2929-34.

Schwartz P, Priori S, Locati E, Napolitano C, Cantu F, Towbin J, Keating M, Hammoude H, Brown A, Chen L and Colatsky T. Long QT syndrome patients with mutations of the *SCN5A* and *HERG* genes have differential responses to Na^+ channel blockade and to increases in heart rate. Implications for gene-specific therapy. ***Circulation,*** 1995; 92:3381-6.

Wang Q, Curran ME, Splawski I, Burn TC, Millholland JM, VanRaay TJ, Shen J, Timothy KW, Vincent GM, de Jager T, Schwartz PJ, Towbin JA, Moss AJ, AtkinsonDL, Landes GM, Connors TD and Keating MT. Positional cloning of a novel potassium Channel gene: *KVLQT1* mutations cause cardiac arrhythmias. ***Nature Genetics,*** 1996; 12:17-23.

Olson TM and Keating MT. Mapping a cardiomyopathy locus to chromosome 3p22-p25, ***Journal of Clinical Investigation,*** 1996; 97:528-32.

Spector PS, Curran ME, Keating MT and Sanguinetti MC. Class III antiarrhythmic drugs block HERG, a human cardiac delayed rectifier K^+ channel open-channel block by methanesulfonanilides. ***Circulation Research,*** 1996; 78:499-503.

Connors TD, Burn TC, Millholland JM, Van Raay TJ, Wang Q, Shen J, Splawski I, Curran ME, Keating MT and Landes GM. Combining exon trapping with gene trapper™: rapid identification and cloning of the KVLQT1 gene. ***Focus***, 1996; 18:31-32.

Sanguinetti MC, Curran ME, Spector PS and Keating MT. Spectrum of HERG K^+ channel dysfunction in an inherited cardiac arrhythmia. ***Proceedings of the National Academy of Sciences (USA)***, 1996; 93:2208-12.

Dumaine R, Wang Q, Keating MT, Hartmann HA, Schwartz PJ, Brown AM and Kirsch GE. Multiple mechanisms of Na+ channel-linked long-QT syndrome. ***Circulation Research***, 1996; 78:916-24.

Spector PS, Curran ME, Zou A, Keating MT and Sanguinetti MC. Fast inactivation causes rectification of the I_{Kr} channel. ***Journal of General Physiology***, 1996; 107:611-19.

Wang Q, Li Z, Shen J and Keating MT. Genomic organization of the human *SCN5A* gene encoding the cardiac sodium channel. ***Genomics***, 1996; 34:9-16.

Frangiskakis JM, Ewart AK, Morris CA, Mervis CB, Bertrand J, Robinson BF, Klein BP, Ensing GJ, Everett LA, Green ED, Proschel C, Gutkowski NJ, Noble M, Atkinson DL, Odelberg SJ and Keating MT. *LIM-kinase*1 hemizygosity implicated in impaired visuospatial constructive cognition, ***Cell***, 1996; 86:59-69.

Compton S, Lux R, Ramsey M, Strelich K, Sanguinetti M, Keating M and Mason J. Genetically defined therapy of inherited long QT syndrome: correction of abnormal repolarization by potassium. ***Circulation***, 1996; 94:1018-22.

Sanguinetti MC, Curran ME, Zou A, Shen J, Spector PS, Atkinson DL and Keating MT. Coassembly of KvLQT1 and minK (IsK) proteins to form cardiac I_{Ks} potassium channel. ***Nature***, 1996; 384:80-3.

Zou A, Curran ME, Keating MT, and Sanguinetti MC. Single HERG delayed rectifier K+ channels expressed in *Xenopus* oocytes. ***American Journal of Physiology***, 1997; 272:H1309-14.

Splawski I, Timothy KW, Vincent GM, Atkinson DL and Keating MT. Molecular basis of the long-QT syndrome associated with deafness. ***New England Journal of Medicine***, 1997; 336:1562-67.

Li DY, Toland AE, Boak BB, Atkinson DL, Ensing GJ, Morris CA and Keating, MT. Elastin point mutations cause an obstructive vascular disease, supravalvular aortic Stenosis. ***Human Molecular Genetics***, 1997; 6:1021-28.

Orias M, Bray-Ward P, Curran ME, Keating MT and Desir GV. Genomic localization of the human gene for KCNA10, a cGMP-activated K channel. ***Genomics***, 1997; 42:33-7.
Keating MT. Reply: Molecular basis of the long-QT syndrome, ***New England Journal of Medicine,*** 1997; 337:1012-3.

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